Report

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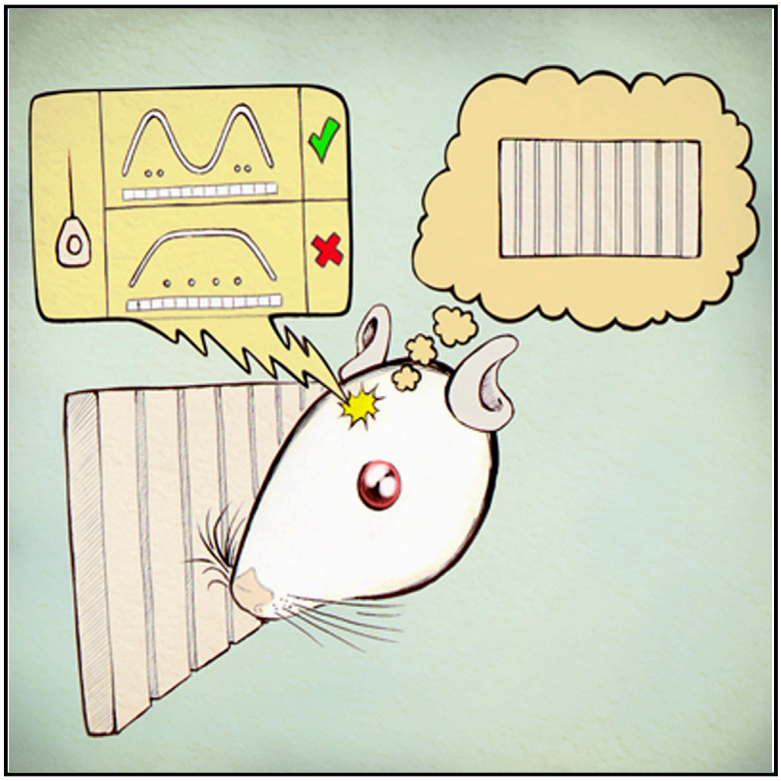
# Complementary Contributions of Spike Timing and Spike Rate to Perceptual Decisions in Rat S1 and S2 Cortex

## Graphical Abstract



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## In Brief

Spike timing and spike rate make complementary contributions to perceptual decisions in rat S1 and S2 cortex. Zuo et al. examine neuronal spike trains in somatosensory cortex as rats whisk on surfaces to identify texture. Both the rate and temporal distribution of spikes carry stimulus information, but the signal in spike timing is greater and better predicts the animal's percept. Rate and timing are complementary codes that govern perception.

## Highlights

- We compared spike rates and spike timing as neuronal codes for texture perception
- Spike timing carried more texture information than spike rates did
- The information in spike timing better predicted the animal's perceptual decision
- Rate and timing are complementary multiplexed neuronal codes that govern perception

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Report

# Complementary Contributions of Spike Timing and Spike Rate to Perceptual Decisions in Rat S1 and S2 Cortex

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## Summary

**When a neuron responds to a sensory stimulus, two fundamental codes [1–6] may transmit the information specifying stimulus identity—spike rate (the total number of spikes in the sequence, normalized by time) and spike timing (the detailed millisecond-scale temporal structure of the response). To assess the functional significance of these codes, we recorded neuronal responses in primary (S1) and secondary (S2) somatosensory cortex of five rats as they used their whiskers to identify textured surfaces. From the spike trains evoked during whisker contact with the texture, we computed the information that rate and timing codes carried about texture identity and about the rat's choice. S1 and S2 spike timing carried more information about stimulus and about choice than spike rates; the conjunction of rate and timing carried more information than either code alone. Moreover, on trials when our spike-timing-decoding algorithm extracted faithful texture information, the rat was more likely to choose correctly; when our spike-timing-decoding algorithm extracted misleading texture information, the rat was more likely to err. For spike rate information, the relationship between faithfulness of the message and correct choice was significant but weaker. These results indicate that spike timing makes crucial contributions to tactile perception, complementing and surpassing those made by rate. The language by which somatosensory cortical neurons transmit information, and the readout mechanism used to produce behavior, appears to rely on multiplexed signals from spike rate and timing.**

## Results

### Performance of Rats in the Texture Discrimination Task

To investigate how candidate somatosensory coding mechanisms contribute to behavior, we trained five rats to turn to the left or right reward spout according to the texture (smooth and 1, 2, and 4 mm groove spacing) they palpated with their whiskers (Figures S1A and S1B). Because the difficulty of categorization might depend on the textures' physical properties—for instance, it may be easier to distinguish textures with disparate spatial features—we varied the discrimination task across rats (Table S1). Figure S1C shows that the overall behavioral performance averaged over rats was 76.9% and was better than chance (paired t test versus chance performance; $p < 0.001$).

### Contact of Whiskers with Textures and the Consequent Neuronal Responses in S1 and S2

Using intracranially implanted tetrodes (Figure S1D) in five rats, we recorded the firing of 459 neurons from S1 (164 of them judged as single units) and 263 from S2 (87 judged as single units), where the term "neuron" refers to both single units and multiunits. Simultaneously, we collected high-speed (one image per ms) videos of whisker movement during texture exploration.

We first analyzed the videos to extract the times of whisker contact with the plate (Figure S1B). For spike train analysis in each touch, the analysis window began with first contact of any whisker and ended when all whiskers broke off contact. Compatible with previous reports [7–9], rats typically made a small number of touches per trial (median 3; interquartile range 2) before withdrawing. The median duration of a single touch was 44 ms (interquartile range 41 ms). Rats exhibited the same distribution of touch parameters for the different textures (Mann-Whitney-Wilcoxon tests; $p > 0.05$), suggesting that motor output was not modulated by the texture.

We then measured for each neuron the temporal profile of firing, averaged over all touches and textures, following the time of contact of the whiskers with the plate. This revealed a sharp rise in instantaneous spike rate after contact (Figure S1E), with a latency of 4 ms in S1 and 8 ms in S2 (paired t test versus baseline; $p < 0.0005$; Bonferroni corrected in both cases).

### Information Carried by Spike Rates and Spike Timing during Correct Behavior

In the first analysis, we considered stimulus coding only in trials with correct choice. We dissected, in each trial, the time-averaged spike rate signal from the spike-timing texture signal, and we then measured the information [10] about texture carried by rate and timing, separately and in conjunction. To do so, we computed the projection (or "score") of the spike train recorded on each touch onto two texture-discrimination templates. The "rate template" (Figures 1A and 1B) is a flat template with nonzero mean. The projection onto it is equivalent to the simple count of spikes in each touch, and thus, the rate template extracts exclusively rate information. The "timing template" (Figures 1A and 1B), constructed using principal components, has a temporal shape achieving optimal correct-trial discrimination among textures once single-touch spike times are projected onto it. Unlike the rate template, the timing template has a zero mean, and as such, it is largely insensitive to rate information (Supplemental Information). This measure of spike-timing information

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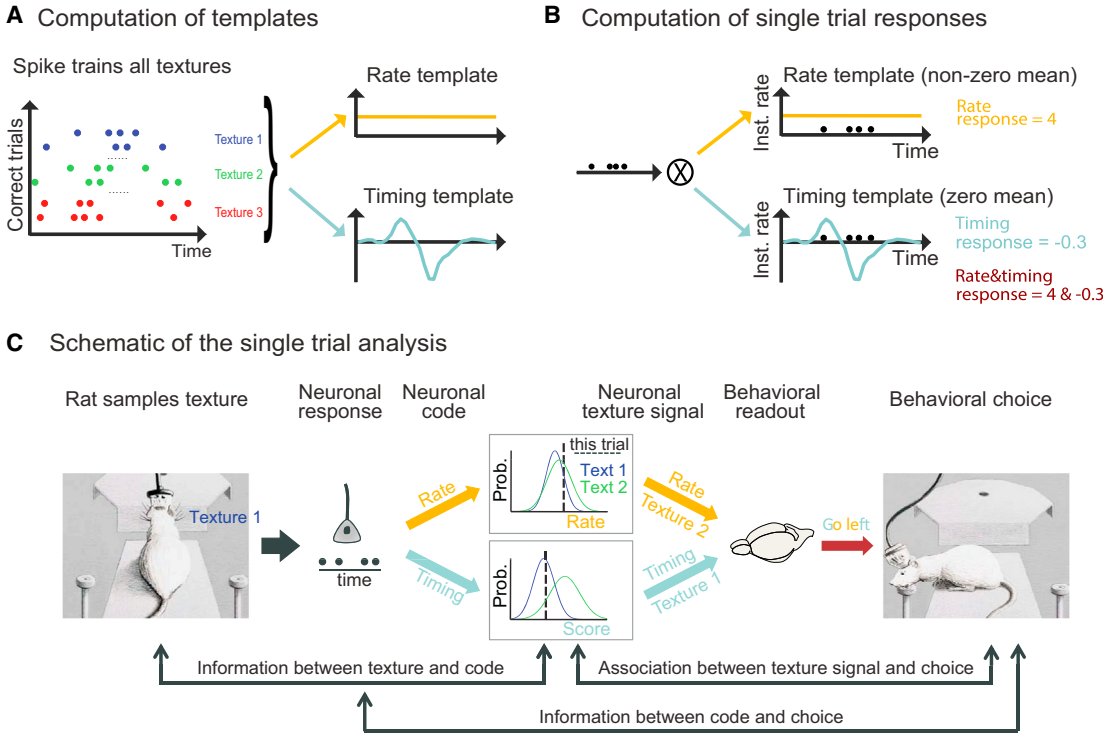


Figure 1. Schematic Illustration of the Analytical Procedures

(A) Computation of templates. Separately for each neuron, using spike trains from all correct trials in response to all textures (left panel), we apply a principal-components-based procedure to extract rate-based and timing-based templates (upper and lower right panels, respectively). From these templates, we extract information about the texture signal in each trial. The rate template is constant over time and captures any texture-specific differences in rate on a scale of the entire measurement window. The timing template is constructed with millisecond-scale temporal resolution but zero mean over time; it captures information present in the spike times.

(B) Quantification of single-trial response according to three neuronal codes. Projection (X symbol) of the single-trial spike train onto the (flat) rate template yields the spike count (rate code). Projection of the spike train onto the timing template yields a number, or "score," describing the temporal position of the spikes (timing code). In this example, the negative score indicates that most spikes occurred at temporal locations with a negative weight on the temporal template. We also obtained a third neuronal code (joint rate and timing), formed by pairing the spike count and temporal scores obtained from the same spike train.

(C) Computation of information and single-trial decoding. Our conceptual model is that when the rat samples the texture (left panel), whisker motion is transduced into a neuronal response (second-from-left panel) that carries information by a rate and/or timing code (middle panel). Behavioral readout mechanisms integrate rate and timing signals, each of which carries a complementary message (second panel from right). Decision-making centers select a behavioral choice (right panel) based on this information. The stages of processing that are assessed by single-trial measures are shown at the bottom by arrows.

differs from common measures of timing information that include the effect of both timing and rate and whose lower bound is the rate information [5, 6, 11, 12]. If the responses of a neuron contain rate information but have no reliable temporal structure, the rate template will extract information but the timing template will not (Supplemental Information). Because of these properties, our template-projection procedure distinguishes between two potentially complementary sensory information channels (rate and timing) that might simultaneously operate within the same spike train.

Figure 2 illustrates the analysis performed on a representative S2 single unit using a 0–30 ms postcontact window. The raster plot (Figure 2A) and the instantaneous firing rate profile (Figure 2C) show the texture-dependent timing of the response. In correct trials, the 4 mm texture elicited higher firing than other textures at short latency (5–10 ms after touch onset), whereas the smooth texture elicited higher firing later (12–20 ms after touch onset). The template derived for this neuron (Figures 2E and 2F) captured these texture-dependent profiles, assigning negative scores to the 4 mm texture, positive scores to the smooth texture, and intermediate scores to the 1 mm texture (Figure 2G). In contrast, the time-averaged firing rate for this neuron varied little across textures, allowing a poorer discrimination capacity (Figure 2G). An S1 single unit, showing similar properties of rate and timing coding, is shown in Figure S2.

To evaluate texture coding in the complete data set, we used the texture-specific distributions of single-touch rate and timing scores (Supplemental Information) to measure the texture information carried, on correct trials, by spike rate and spike timing for all neurons (both single and multiunits) in S1 and S2. The average information per touch allowed us to compare the candidate coding mechanisms on the same scale in an unbiased manner. For this and all following analyses, we selected neurons (299/459 from S1 and 154/263 from S2) that carried significant texture information ($p < 0.05$; permutation test) either by rate or timing (Supplemental Information) and we considered a touch time window extending 50 ms after initial contact. This window extended to the initial portion of the subsequent touch in only 6% of cases. (Figures S3A and S3B evaluate how information evolved along the course of the touch, from 20 to 50 ms.)

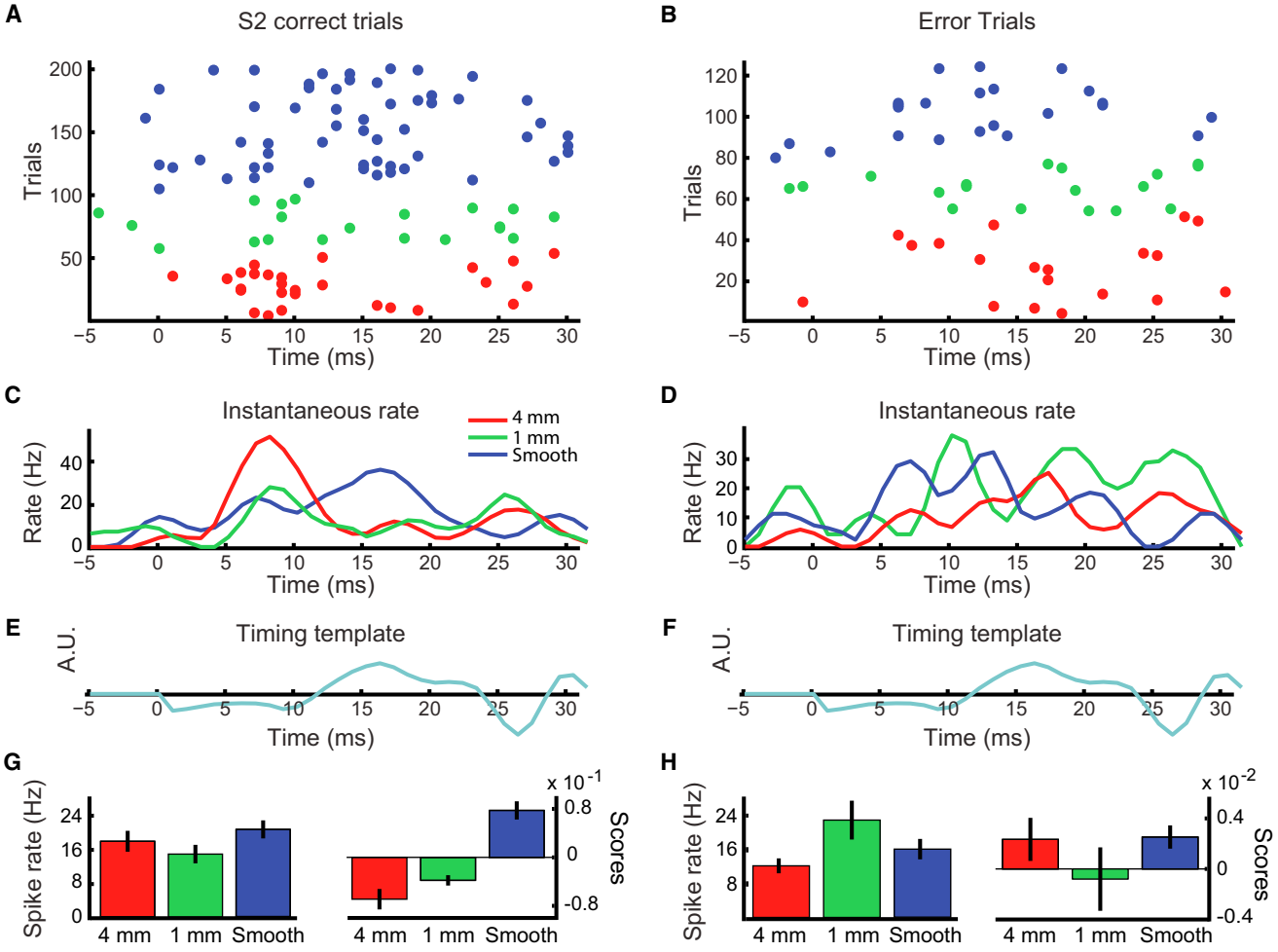


Figure 2. Texture-Dependent Temporal Structure of an Example S2 Neuron

Responses of a representative single unit in S2 are shown over a time window from −5 to 30 ms relative to contact onset. Throughout the figure, responses to different textures are color-coded as follows: smooth (blue); 1 mm (green); and 4 mm (red).

(A) Raster plot of the neuron on correct trials. Trials are arranged in blocks according to texture presented. Because the neuron did not fire on every trial, trials with no spikes are not plotted.

(B) Same as (A) for error trials.

(C) Instantaneous firing rates constructed as trial-averaged spike trains (smoothed with 2 ms Gaussian) to reveal the time-varying spiking profile associated with each texture.

(D) Same as (C) for error trials.

(E and F) Shape of the timing template for correct texture discrimination obtained on correct trials for this neuron. To help visualization, the same template is repeated in both panels. A.U., arbitrary units.

(G) Left panel: mean ± SEM across trials of spike rates evoked by the different textures. Right panel: mean ± SEM across trials of scores of the temporal response to the different textures.

(H) Same as (G) for error trials.

The average texture information per touch carried by spike rate and spike timing on trials with correct behavior is reported in Figures 3A and 3B for single units and multiunits separately and then for the merged set of all neurons. Because the timing information was at least as large as rate information for both single and multiunits, from here onward we describe findings for the merged data. In that data set, the information in timing was significantly higher than that in rate ($p < 0.05$; paired t test). The amount of timing information was larger for S1 than for S2 neurons ($p < 0.05$; paired t test).

The shape of timing templates for example neurons (Figures 2E, 2F, S2E, and S2F) and for the full population (Figures S2I and S2K) demonstrates that correct texture discrimination could be based on millisecond-scale differences in texture-specific spike timing. To characterize the temporal precision of the code, we examined texture information after shuffling spike times within varying window sizes (Supplemental Information). A significant quantity of information was lost when the shuffling was as small as 2 ms (for S1) and 5 ms (for S2; Figure S2J), confirming texture information encoding at millisecond scale.

Intuitively, if rate and timing carried largely independent signals about texture, their joint "rate and timing" information should be close to the sum of their individual quantities. Figures 3A and 3B show that, for both single and multiunits (and for all postcontact time windows considered; Figures S3A and S3B), the rate and timing texture information was not statistically different from the sum of rate and timing information

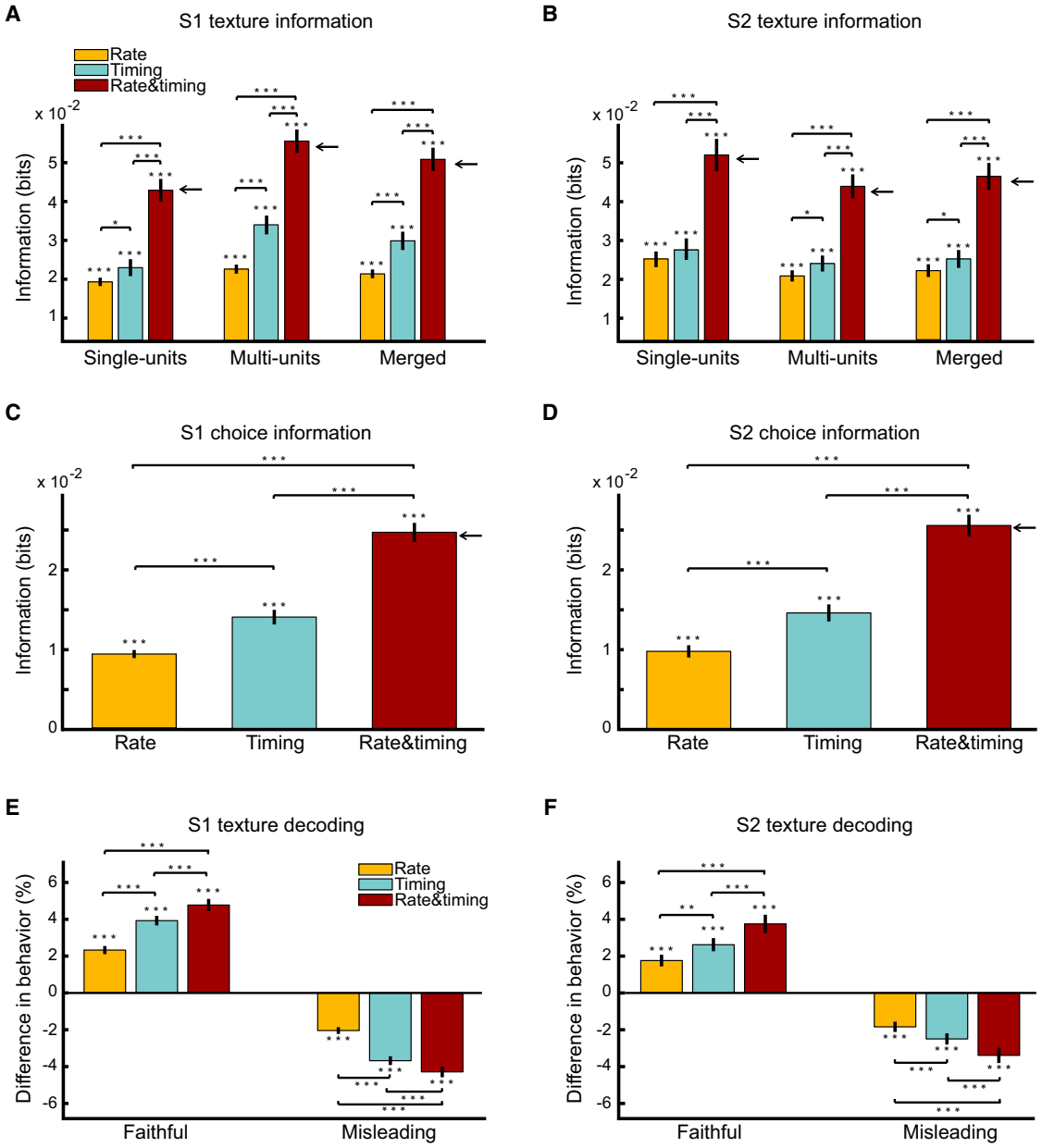


Figure 3. Texture Information Carried by S1 and S2 Spike Rates and Spike Timing and Their Relationship with Behavioral Outcome

All results derive from a 0–50 ms window after touch onset and are plotted as mean (with error bars indicating SEM) over the population of neurons carrying a significant quantity of texture information. Left panels are S1 neurons, right panels S2 neurons. *p < 0.05, **p < 0.01, ***p < 0.001.

(A) Information about texture carried by S1 spike rates, spike timing, and rate and timing during correct behavior. For single units, multiunits, and all units merged, the information carried by timing was greater than that carried by rate (paired t test). The information carried by joint rate and timing was in all cases not different (p > 0.4; paired t test) from the sum of the information carried by rate and timing separately (adjacent horizontal arrows), suggesting that timing and rate code function as largely complementary sensory information channels.

(B) Information about texture carried by S2 spike rates, spike timing, and rate and timing during correct behavior, using the same format as (A). For all data sets, the information in timing was at least as high and sometimes higher (paired t test) than the rate code. Again, the information in joint rate and timing was in all cases not different (p > 0.4; paired t test) from the sum of the information carried by rate and timing codes separately (horizontal arrows).

(C) Information about behavioral choice by S1 spike rates, spike timing, and rate and timing. The information carried by rate and timing was significantly higher than that carried by either rate or timing alone (paired t test).

(D) Same analysis as (C) for S2 neurons.

(E) The change in probability of correct behavioral choice when information in a given neuronal code (rate, timing, or rate and timing) of an S1 neuron was either faithful (i.e., correct texture was decoded) or misleading (i.e., incorrect texture was decoded).

(F) Same analysis as (E) for S2 neurons.

(p > 0.5; paired t test). Additional work (Supplemental Information) showed that the approximately linear summation of information arose because signal and noise correlations between the two codes were small. The available evidence is thus consistent with the approximate independence of rate and timing codes, though not a proof.

In conclusion, cortical neurons multiplex texture signals through rate and timing—complementary sensory information channels that operate on different time scales.

### Influence of Single-Touch Rate and Timing Information on Animal Choice

Although the information in both rate and timing is available to successive stages of processing, their mere presence does not assure a contribution to perception: signals may be lost in the stages of processing that lead to an eventual decision. Evidence of the direct conversion of spike rate and timing to the animal's choice can be assessed by analytically comparing neural responses in correct trials to those in error trials (shown in Figures 2 and S2 for two example neurons). To do so, we employed a range of approaches (Figure 1C).

First, we measured how much information about the rat's choice (be it correct or incorrect) could be extracted from the spike trains preceding that choice. If the behavioral readout mechanism utilized only a single code (e.g., rate), then the complementary code (e.g., timing) could supply no additional information. In contrast, if downstream centers utilized both codes, then the information available about choice in the two signals together would surpass that in either code alone and could even approach their summated value. To select between these models, we used correct and error trials to compute the information about the behavioral choice carried by rate, timing, and their combination (rate and timing). The joint knowledge of rate and timing carried more information about choice than either code alone (Figures 3C and 3D; paired t test; $p < 0.001$), indicating that the behavioral readout mechanism utilized both rate and timing. Additional findings emerged from this test. The larger ($p < 0.001$) amount of choice information carried by timing compared to rate suggests a more important role of spike timing in the behavioral readout. This implication was confirmed by choice probability measures (Figures S3C and S3D). Moreover, the joint rate and timing choice information was not different from the sum of the separate information values ($p > 0.4$; paired t test), indicating that downstream decision-making centers seem to multiplex two complementary messages.

Second, we reasoned that, if a neuron contributes to behavior using a given code, there should be an association on each trial between the accuracy of information provided through that code and behavioral outcome. When the neuron provides accurate evidence through this code, then the likelihood of correct behavior should increase. Conversely, when the neuronal code provides inaccurate evidence, the likelihood of correct behavior should decrease. Hereafter, "faithful" versus "misleading" refers to the accuracy of texture identity transmitted by the considered neuronal code on each touch, whereas "correct" and "error" refer to the animal's behavioral choice on the same trial. We decoded texture using a Bayesian classifier (Supplemental Information). Then, separately for each neuron and for all candidate codes, we divided touch-evoked neuronal responses into those carrying faithful and misleading texture information (i.e., those for which the decoded texture did and did not match the presented texture, respectively). We then computed the change in performance according to whether the information was faithful versus misleading. Change in performance was the difference in percentage of correct behavior across all trials from that predicted by the optimal discrimination when no neuronal information was used for decoding, that is, when texture was decoded only according to its priori probability. For all codes (rate, timing, and joint rate and timing), faithful information in S1 and S2 on a single touch was associated with an increase in the likelihood of correct behavior on that trial; misleading information was associated with a decrease in correct behavior (Figures 3E and 3F). However, the degree of single-trial association between information accuracy and behavior in S1 and S2 was larger ($p < 0.001$; paired t test) for the joint rate and timing code than for either code alone. Timing alone showed a stronger association with behavior than did rate alone ($p < 0.001$; paired t test). On average, the overall difference in behavioral performance between faithful and misleading trials for rate, timing, and rate and timing codes was 4.1%, 7.6%, and 9.1% for S1 and 3.5%, 5.2%, and 7.2% for S2. Together, these results suggest that the behavioral readout mechanism uses rate and timing information in a complementary manner, with timing more influential.

From the above results, a simple prediction naturally arises: that the sensory evidence carried by spike timing weighs more in the rat's behavior than the evidence carried by rate. To evaluate the prediction, we focused on "contradictory" touches—those where the rate and timing signal of a neuron indicated that opposing choices should be made (for example, the textures decoded from rate and timing would be rewarded with a left and a right turn, respectively; Figure S3F). Contradictory touches were 15% of the total number of touches for S1 and 11% for S2 neurons. In the majority of contradictory touches (59% for S1 and 63% for S2), the rat's action sided with the timing code, indicating that the behavioral readout was more likely to obey the code that on average carried more texture information—the timing code (Figures S3E–S3G).

## Discussion

### Linking Sensory Information and Behavior in the Same Trial

Cracking the neuronal codes for perception [13, 14] will ultimately require characterizing, in single trials, (1) the coding mechanisms by which spike trains represent sensory information and (2) the readout mechanisms by which these same spike trains contribute to the subject's decision. Sensory coding and readout for decision making usually have been considered separately: the former with information theory or decoding [10] and the latter with choice probability measures [15, 16]. To shed light on the direct within-trial relationships between stimulus and sensory code, as well as between sensory code and behavior, here we developed a unifying formalism based on single-trial information theory and decoding [10]. This new methodology opens up two avenues for probing the chain of events from sensory code to behavioral readout. First, it separates the sensory signals in firing rate and in temporal structure. Previous analyses conflated rate and timing contributions, so that timing signals could be inferred only as the additional information available when considering spike trains at finer time resolution [5, 6, 11, 12, 14, 17]. Second, once the stimulus is decoded according to both coding candidates, the decoded message can be compared to the sensory world (the actual stimulus) and to the animal's final percept (revealed by its behavioral choice).

Previous work showed that spike rates correlate with the percept evoked by a stimulus [7, 15, 18]. Our new formalism allowed a direct comparison of the roles of both rate and timing on an animal's percept in the same set of trials, leading to two key insights: (1) sensory information is multiplexed through two complementary mechanisms, spike rate and

millisecond-scale spike timing and (2) complementary sensory evidence borne by rate and timing is combined to produce a behavioral decision. Of the two mechanisms, timing carries more sensory information and has a greater influence on the animal's choice.

### Probing Neuronal Codes during Active Naturalistic Sensory Sampling

The whisker sensory system of rats is an ideal platform for studying how the brain represents sensory stimuli and, subsequently, transforms such representations into percepts guiding the animal's decisions [19, 20]. The speed and accuracy of their texture judgments [7–9] indicate that neurons employ efficient coding mechanisms. Previous work showed that millisecond-scale S1 firing patterns encode whisker stimuli in anesthetized animals [6, 11]. Here, we show that firing patterns are also present during active perception and are relayed to the behavioral readout stage.

In our experiment, freely moving rats exercised "generative sensation" [21] under their own control. The advantage of such conditions is that the brain is actively engaged in a more natural task. The complication is that, under naturalistic conditions, it is difficult to separate the contribution to spike rate and timing variability of extrinsic sources (i.e., the differences across trials and across whisks in the rat's motor output and the consequent interaction of the whiskers with the texture) [22, 23] and of intrinsic sources (i.e., state fluctuations of the engaged neuronal circuitry) [24]. Nevertheless, naturalistic conditions (compared to those in immobilized animals) allowed us to show that the neuronal "signatures" of each stimulus—the stimulus-dependent differences in both rate and timing—were robustly enough encoded and decoded to survive the sensorimotor system's intrinsic and extrinsic variability.

An alternative strategy is to study causally the role of neuronal codes by exciting or suppressing neuronal activity with optogenetics or electrical stimulation [25–29]. The insertion of neuronal signals into cortex has been effective in behavioral tasks, such as detection of pole collision in a whisking, head-fixed mouse [30], where the coding mechanism for the sensory event is approximately uniform across neurons. However, insertion of artificial texture signals into the brain is not yet feasible. To avoid the superimposition of contact-evoked firing with artificial firing, the real texture would have to be substituted by a virtual one. Because texture perception originates in the rat's own movement, the external excitation would need to be delivered precisely when expected by the rat. Nevertheless, the dictionary of rates and patterns emerging from the current work (Figure S2I) brings the possibility of artificial sensation closer.

### The Code Used for Perceptual Judgments across Stages of Processing

The spike timing uncovered here likely reflects kinematic signatures of texture-specific whisker motion [8, 22] rather than the internal dynamics of cortical circuits. It has been argued that intrinsic constraints of cortical architecture prevent the preservation of precise timing information beyond peripheral levels and the first cortical stage [31, 32]. To learn whether information in spike timing is conserved beyond the first cortical stage, we also recorded activity from S2. The function of S2 in rodents has been an issue of longstanding debate [33–35]. Besides providing the first description of the texture-encoding properties of S2 neurons in behaving rodents, our results show that millisecond-scale timing carries at least half of the spike train's total information across successive stages of the cortical hierarchy.

### Connection between Neuronal Codes and Tactile Perception

A comparison of coding mechanisms for tactile perception was accomplished in studies where monkeys discriminated between vibrations in the range of 8–36 Hz [36]. Most S1 neurons encoded vibration frequency by firing rate; still, a large proportion of neurons discharged in phase with each skin deflection, leading to a potential spike-timing code for vibration frequency. Firing rate was better related to perception than was firing pattern [18]. However, the discrimination between higher frequency (>100 Hz) vibrations might employ a temporal code in S1 multiplexed with a rate code [37]. The analytical approach developed here will make it possible to systematically weigh the single-trial contribution of the two candidate coding mechanisms to sensory perception in all modalities.

## Conclusions

All findings reported suggest that sensory information is multiplexed into complementary codes—spike rate with a resolution of tens of milliseconds and spike timing with a resolution of few milliseconds. The complementary evidence from rate and timing is combined and used for behavioral decisions, with timing providing the stronger overall contribution.

### Supplemental Information

Supplemental Information includes Supplemental Experimental Procedures, three figures, and one table and can be found with this article online at http://dx.doi.org/10.1016/j.cub.2014.11.065.

### Author Contributions

S.P. and M.E.D. conceived the scientific question. Y.Z., H.S., S.P., and M.E.D. designed the study. Y.Z. and H.S. performed research. Y.Z., H.S., G.N., A.M., S.P., and M.E.D. contributed materials and methods. S.P. and M.E.D. wrote the manuscript. Y.Z., H.S., G.N., A.M., S.P., and M.E.D. commented on the manuscript.

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